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**Emotional maltreatment is associated with atypical responding to  
stimulation of endogenous oxytocin release  
through mechanically-delivered massage in males**

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## Abstract

The neuropeptide oxytocin plays an important role in social behavior, parenting, and affectionate touch. Previous research has shown that massage stimulates oxytocin release. However, the effect of massage without human touch is unknown. We examined the effects of massage applied by a massage seat cover on salivary oxytocin levels in two exploratory pilot studies using within-subject designs. In Study 1 massage effects on oxytocin levels were examined in a sample of  $N = 20$  healthy female participants. Effects of a 15-minute massage session were compared to a control condition during which participants sat on a comfortable chair without a massage seat cover. Salivary oxytocin levels were measured at baseline and up to three hours after the session. Massage applied by the seat cover increased salivary oxytocin levels compared to the control condition, indicating that human touch is not an essential component in the oxytocin enhancing effects of massage. In Study 2, we examined whether effects of massage in  $N = 46$  healthy male participants depend on experiences of emotional maltreatment. In addition, we examined whether enhanced oxytocin levels after massage affect the use of excessive handgrip force in response to infant crying and laughter as measured with a handgrip dynamometer. We found that high oxytocin levels after massage were related to reduced handgrip force during exposure to infant crying and laughter, indicating that massage stimulates a sensitive response to infant signals by stimulating oxytocin release. However, men with experiences of emotional maltreatment showed lower oxytocin levels, which did not increase after massage. Our findings indicate that emotional maltreatment is associated with atypical responding to stimulation of endogenous oxytocin release.

Keywords: oxytocin, massage, affectionate touch, massage seat cover, emotional maltreatment, infant signals

## Introduction

The neuropeptide oxytocin is well known for its role in social affiliation, parenting, and other forms of social behavior (Carter, 1998; Feldman, 2012; Feldman & Bakermans-Kranenburg, 2017). Research has shown that it is involved in initiating the “touch circuitry” between parents and infants and that human touch or massage can stimulate oxytocin release (Gordon et al., 2010). For example, maternal oxytocin levels increased after infant contact in mothers who provided high levels of affectionate touch (Feldman et al., 2010). Maternal oxytocin has also been shown to be enhanced when newborns perform massage-like hand movements to the mothers’ breast in preparation for the first breastfeeding (Matthiesen et al., 2001).

Other studies point to oxytocin enhancing effects of massage in adults. Holt-Lunstad et al. (2008) found that married couples who received a 4-week intervention to increase support through warm touch (touching their partner’s neck, shoulders, and hands) showed increased salivary oxytocin levels compared to a control group. In line with these findings, Morhenn et al. (2012) found that massage increases plasma oxytocin and reduces adrenocorticotropin hormone, possibly indicating that massage has stress-reducing and anxiolytic effects. Although there is some evidence that massage stimulates endogenous oxytocin release, there may be individual differences in the response to massage or affectionate touch. Effects of massage may be different for men and women because of sex differences in the oxytocin system (Taylor, 2006); men have been shown to have higher plasma oxytocin levels than women (Weisman et al., 2013) and respond differently to exogenous intranasal oxytocin administration (Rilling et al., 2014).

Another individual difference factor that may influence the endogenous oxytocin release is childhood caregiving experiences. Childhood caregiving experiences play an important role in shaping the oxytocin system (Feldman, 2015) and influence oxytocin release

in response to stress (Pierrehumbert et al., 2010). In addition, childhood caregiving experiences have been shown to affect sensitivity to intranasal oxytocin in multiple studies. For example, we found that intranasal oxytocin administration decreased the use of excessive handgrip force in response to infant crying, but only in individuals who reported positive childhood experiences and not in individuals who reported harsh caregiving experiences (Bakermans-Kranenburg et al., 2012). Negative childhood experiences also moderate oxytocin effects at the neural level: oxytocin effects on resting-state functional connectivity were only found in individuals who reported a supportive family background (Riem et al., 2013). In a similar vein, Meinlschmidt and Heim (2007) showed that individuals with experiences of early parental separation exhibited attenuated cortisol decreases after intranasal oxytocin administration (versus placebo) compared with control subjects without experiences of early separation. Furthermore, individuals with negative childhood experiences show lower oxytocin levels in cerebrospinal fluid (Heim et al., 2009) and plasma (Opacka-Juffry & Mohiyeddini, 2012), indicating that adverse childhood experiences may lead to a dysregulation of the oxytocin system. Individuals with negative childhood experiences may therefore also show abnormal responding to stimulation of endogenous oxytocin release through massage.

In the current studies, we examine whether massage stimulates endogenous oxytocin release in men and women and whether enhanced oxytocin levels after massage affect responses to infant crying and laughter. In a previous study, we found that intranasal oxytocin modulates neural responses to infant crying: oxytocin increased reactivity in empathy-related brain regions and decreased amygdala reactivity to crying (Riem et al., 2011). Similarly, reduced amygdala activity after intranasal oxytocin administration was also found during exposure to infant laughter (Riem et al., 2012). Reduced amygdala activity may be the mechanism underlying the anxiolytic and stress-reducing effects of oxytocin, which promote

a sensitive caregiving response to an infant signal. This is particularly important during exposure to infant crying, as crying can elicit negative feelings of aversion and anger (Soltis, 2004) and excessive infant crying can even elicit harsh caregiving responses in some parents (Barr et al., 2006; Reijneveld et al., 2004). It is however unknown whether stimulation of endogenous oxytocin release influences responding to infant crying and laughter.

Another important question is whether human touch is an essential component of the oxytocin enhancing effects of massage. A previous study found that human touch had a sharpening effect on social evaluations of human faces compared to machine touch, but only after intranasal oxytocin administration (Ellingsen et al., 2014). The current study is the first to examine whether massage *without* human touch elevates oxytocin levels. We examine the effects of massage applied by a massage seat cover on salivary oxytocin levels in two exploratory pilot studies. In Study 1 massage effects on oxytocin levels are examined in a sample of  $N = 20$  healthy female participants. We expected that massage stimulates endogenous oxytocin release and results in increased oxytocin levels. In Study 2, we examine whether effects of massage in  $N = 46$  healthy male participants depend on experiences of emotional maltreatment. In addition, we examine whether enhanced oxytocin levels after massage affect the use of excessive handgrip force in response to infant crying and laughter as measured with a handgrip dynamometer. We expected that enhanced oxytocin levels after massage are related to decreased handgrip force in response to infant signals, but that oxytocin-releasing effects of massage are influenced by emotional maltreatment.

## Study 1

### Methods

#### *Participants*

Participants were 20 females who volunteered to participate in the current study. The mean age of the participants was 27.50 years ( $SD = 6.53$ , range 22-46). The majority (60%) used oral contraceptives and did not have children of their own (90%). The study was approved by the Ethics Committees of the Institute of Education and Child Studies of Leiden University. Participants were invited for the study in the luteal phase of their menstrual cycle in order to control for hormonal influences due to the menstrual cycle. For one participant it was not possible to determine menstrual phase because of use of intrauterine device. Exclusion criteria were arm, neck, and back injuries, pregnancy, breastfeeding, and use of medications other than oral contraceptives. All participants were non-smokers.

### *Procedure*

Participants were invited for lab sessions on two successive days. They were instructed to abstain from alcohol and excessive physical activity during the 24 hours before the start of study, and from caffeine on the data collection days. The sessions started at 9:00 a.m. with saliva collection to assess baseline OT levels. Participants completed questionnaires on food and drink intake, physical exercise, mood, and stress. Participants were then instructed to sit either on a chair with the electric massage seat cover (massage condition) or on the same chair without the seat cover (control condition) for 15 minutes while looking at photographs of landscapes. Neck, shoulders, and back were massaged by the seat cover (type: Medisana 88930). The massage and control conditions were counterbalanced. Afterwards, saliva was collected at 9:15, 10:00, 11:00, and 12:00 a.m. and the mood questionnaire was completed again at 9.15 and 12.00 a.m. Participants left the laboratory after the second saliva collection but were asked to stay around in order to provide saliva samples at 10:00, 11:00, and 12:00 a.m.

### *Questionnaires*

Current mood was measured with the Positive Affect Negative Affect questionnaire (PANAS; Watson, Clark, & Tellegen, 1988). These items include 10 items for positive affect (e.g., alert, enthusiastic, determined) and 10 items for negative affect (e.g., upset, irritable, nervous). Each item was rated on a 5-point scale ranging from 1 = not at all to 5 = a lot. We used the Positive Affect scale ( $\alpha > .85$ ), indicating positive mood before and after sitting on the (massage) chair. In addition, participants rated on two 10-point rating scales how much stress they experienced at home and at work on the day of the lab session. We used work-related stress as covariate, because OT levels were measured at work.

### *Salivary oxytocin*

At least 1 ml of unstimulated saliva was collected into cryotubes for each sample using the passive drool method. Samples were immediately frozen and were stored at  $-20^{\circ}\text{C}$  until batch assay. Level of OT in saliva was assayed using a commercially available kit as per the method previously described and used before (Grewen et al., 2010). Prior to the enzyme immunoassay procedure, in keeping with the manufacturer's strong recommendation, an extraction step was performed based on instructions accompanying the EIA kit available in February 2011 (ADI-900-153, Enzo Life Science, Plymouth Meeting, PA, USA). OT extraction efficiency was 94%. The lower limit of sensitivity was 1 pg/ml. 6.5% of the samples fell below the lower level of sensitivity. These values were replaced with 0.90 pg/ml. The intra- and inter-assay coefficients of variation were 7.56 and 8.20% respectively. The manufacturer reports that cross-reactivity with similar mammalian neuropeptides is less than 1%. Data was screened for outliers but there were none.

### *Data analysis*



We analyzed the repeated measures of OT with multilevel models, using the MIXED procedure in SPSS 21.0 (IBM Corp., 2012). Models were built step-wise, starting from a random intercept model with only linear time as a predictor. A random slope for time and effects of massage condition, work-related stress, and mood were added successively. Time was coded as -0.25, 0, 0.75, 1.75, 2.75, mimicking the actual time frame of measurement, and defining the moment just after massage in the experimental condition as the reference point. We coded condition as a time-varying covariate, with values 0, 1, 1, 1, 1 in the experimental, and 0, 0, 0, 0, 0 in the control condition. This coding allowed for a “skip” in the linear regression line at 9.15 (right after the massage) in the experimental condition (see McCoach & Kaniskan, 2010). Continuous predictors (mood and stress) were centered at the grand mean.

We report unstandardized regression weights  $\beta$  and variance components. To assess overall model fit, we compared nested models using the -2 log likelihood test. To ensure the validity of this test, we used Full Maximum Likelihood estimation. Significance of model parameters was assessed by *t*-tests for the fixed part, and Wald Z-tests for the random part.

## *Results*

The observed OT levels at the five measurement points in the massage and control condition are displayed in Figure 1. Note that there seems to be a “skip” in the regression line at 9:15 a.m. in the massage condition, but only after 10:00 a.m. the values in this condition were structurally higher compared to the control condition.

In Table 1, the results for the estimated multilevel models are displayed. Model 1 only incorporates linear development in OT across time, which can be specified as follows:

$$\text{Level 1: } Y_{ti} = \pi_{0i} + \pi_{1i}(\text{time}) + e_{ti}$$

$$\text{Level 2: } \pi_{0i} = \beta_{00} + u_{0i}$$

$$\pi_{1i} = \beta_{10}$$

The conditional intra-class correlation equals  $1.56 / (1.56 + 1.91) = 0.45$ , indicating that 45% of the variation in the data was on the inter-personal level, after controlling for linear development across time. Note that the intercept refers to the predicted average OT level at 9:15, and varied significantly across persons. Overall, there was a slight linear increase in predicted OT levels across time.

Model 2 shows that neither the random slope for time nor the slope-intercept covariance was significant, indicating no significant inter-personal differences in development of OT levels across time. Thus, following models do not incorporate a random slope. Model 3 includes the effect of massage condition. After massage, the regression line increased 0.51 pg/ml,  $p = .01$ . In both conditions, there was no significant development in OT across time points,  $\beta = 0.12$ ,  $p = .16$ . Including the interaction between time and massage (Model 4) did not lead to a better fit,  $\chi^2(1) = 0.19$ ,  $p = 0.66$ . Note that when interactions are involved, the coefficient for massage refers to the predicted difference in OT between conditions at 9:15.

Finally, Model 5 did not outperform Model 3,  $\chi^2(3) = 3.23$ ,  $p = .36$ , indicating that work stress was not related to inter-personal differences in OT level, and did not interact with time or condition. Finally, when we included mood in Model 3, no significant effect of this covariate emerged ( $p = .33$ ). As mood was only measured at three time points, the fit of this model was not directly comparable to the other models.

To summarize, we found some evidence that massage applied by the seat cover increased salivary OT levels compared to the control condition. No effects of mood and work related stress were found. Our finding extends previous studies investigating the effects of massage by showing that massage *without* human touch may also elevate OT levels. Thus, human touch seems not an essential component in the OT enhancing effects of massage.

## Study 2

### Methods

#### *Participants*

Participants were 51 male students from Leiden University, The Netherlands ( $n = 16$ ), or the University of Milan, Italy ( $n = 35$ ). The mean age of the participants was 22.39 years ( $SD = 2.37$ , range 18-29) and age did not differ between Italian and Dutch participants ( $t(42) = -.24$ ,  $p = .81$ ). Exclusion criteria were use of medication, arm, neck, and back injuries, and psychiatric disorder. Participants did not have children. The study was approved by the Ethics Committees of the Institute of Education and Child Studies of Leiden University. Participants who did not abstain from coffee or alcohol or had wounds in their mouth were excluded from data analyses ( $n = 5$ ), resulting in a final sample of 46 participants. Due to technical problems, handgrip data of two participants in the control condition and seven participants in the massage condition were missing.

#### *Procedure*

Participants were asked to come to the laboratory for participation. They were instructed to abstain from alcohol and excessive physical activity during the 24 hours before the start of study, and from caffeine on the data collection days. Similar to Study 1, the sessions started at 9:00 a.m. with saliva collection (T1) to assess baseline OT levels. Participants completed questionnaires on food and drink intake, physical exercise, mood, and stress. Participants were then instructed to sit either on a chair with the same electric massage seat cover as in Study 1 (massage condition) or on the chair without the seat cover (control condition) for 15 minutes while looking at photographs of landscapes. Neck, shoulders, and back were

massaged by the seat cover (type: Medisana 88930). The massage and control conditions were counterbalanced. Afterwards, saliva was collected at 9:15 (T2), 10:00 (T3), 11:00 (T4), and 12:00 a.m (T5). Between the saliva collection T2 and T3, an experimental infant cry paradigm was administered in order to examine whether enhanced oxytocin levels after massage influences responding to infant signals. Participants were exposed to sounds of infant crying and laughter and were asked to squeeze a handgrip dynamometer (as in Bakermans-Kranenburg et al., 2012). For the purpose of the current study, we focus on saliva collection T1 and T2 to prevent confounding by the handgrip dynamometer task. The procedure of saliva collection and salivary OT analysis was the same as in Study 1.

### *Measurements*

*Mood.* Similar to Study 1 current mood was measured with the PANAS (Watson, Clark, & Tellegen, 1988) (positive affect  $\alpha > .71$ , negative affect  $\alpha > .73$ ).

*Stress.* Participants rated on a 10-point rating scale how much stress they experienced at home.

*Childhood Trauma Questionnaire.* Participants completed the Dutch or Italian version of the Childhood Trauma Questionnaire Short Form (CTQ-SF, Bernstein et al., 1994, 2003). CTQ-SF is a measure of self-reported experiences of childhood abuse. Twenty-eight items were used to assess experiences of physical abuse, emotional abuse, sexual abuse, physical neglect, and emotional neglect. Each item (e.g., “During my childhood I felt hated by family”) was rated on a 5-point Likert scale ranging from never true to very often true. In the current study we focused on the emotional abuse and emotional neglect subscales because these subscales showed largest variability in the current sample. An emotional maltreatment scale was created ( $\alpha = .85$ ) by averaging the 10 items tapping into the emotional abuse and emotional neglect dimensions. The mean score was 1.91 (SD = 0.44) with scores ranging from 1.40 to 3.40. A

log transformation was applied to the emotional maltreatment variable to approach a normal distribution.

*Handgrip force.* A handgrip dynamometer task (Bakermans-Kranenburg et al., 2012; M. M. Riem et al., 2016) was used to examine whether massage affects responding to infant signals. The handgrip dynamometer was used as an indicator of the use of excessive force during listening to infant crying and laughing. Squeeze intensities (in kg) were transferred directly from the dynamometer to the AcqKnowledge software program (version 3.8; Biopac Systems, 2004). Participants were asked to squeeze the handgrip dynamometer as hard as possible and then at 50% of their maximum handgrip strength. They performed as many trials as necessary for training, with their performance displayed on a monitor to check the 50% level of each second handgrip, until they were able to modulate the force of their second squeeze to half the strength of their first squeeze. Then the monitor was directed away from the participant in order to prevent receiving feedback regarding the performance during the remainder of the task. The handgrip-force task was administered on a laptop using E-Prime software (version 2.0; Psychology Software Tools, Inc., PA, USA). During the task participants were seated in front of a computer screen wearing headphones. As a prompt, the words “squeeze maximally” were displayed briefly in the middle of the screen, after 2 s followed by the prompt “squeeze at half strength”, thus prompting the participants to perform a brief firm squeeze followed by a brief squeeze half the strength. After baseline squeezing (no sound), participants were requested to squeeze the handgrip dynamometer eight times at full and half strength, four times during listening to infant laughter and four times listening to infant crying (counterbalanced order). The infant laughter and cry sounds (duration = 2 min) from Groh and Roisman (2009) were used. The intervening time between full- and half-strength prompts was 2 s; the intervening time period between half-strength and the next full-strength prompt was 25 s. Similar to studies on the same and other samples (Bakermans-Kranenburg et al.,

2012; Compier-de Block et al., 2015; M. M. Riem et al., 2016), grip strength modulation was calculated by dividing the half-strength squeeze intensity by the full-strength squeeze intensity, so that scores of over 0.50 indicated excessive force on the half-strength squeeze attempt.

### *Data analysis*

OT levels  $>2$  SD from the mean were considered outliers and were replaced by the maximum value per condition. The correlation between baseline oxytocin level (mean massage and control condition) and emotional maltreatment was assessed. To examine effects of massage on OT levels, differences between OT levels at T1 and T2 in the massage and control condition were calculated. Afterwards, a contrast score was calculated by subtracting the difference score of the control condition from the difference score of the massage condition (Massage (Post – Pre) – Control (Post – Pre)). This contrast score reflects the difference in OT level changes between the massage and the control condition. A hierarchical regression analyses was conducted with the contrast OT score as dependent variable, baseline OT levels (T1) at the day of the massage condition and emotional maltreatment as predictors in the first step and the interaction between baseline oxytocin levels (centered) and emotional maltreatment (centered) in the second step. Further, a repeated measures Anova was performed with time (pre (T1) and post (T2) massage or control chair) and condition (massage, control) as within-subject factors, emotional maltreatment (dichotomized using a median split) and baseline oxytocin levels at the day of the massage condition (dichotomized using a median split) as between-subject factors. Mood and stress were excluded from analysis because these covariates were not significant and did not change the results.

Furthermore, we conducted a repeated measures Anova with handgrip force ratio as dependent variable, condition (massage, control) and infant sound condition (baseline, infant

crying, laughing) as within-subject factors and emotional maltreatment as covariate in order to examine effects of massage on handgrip force in response to infant crying and laughter.

Hierarchical regression analysis with handgrip force ratio during infant crying in the massage condition as the dependent variable was performed to examine whether higher oxytocin levels after massage predict handgrip force in response to infant crying and laughter.

Emotional maltreatment and oxytocin levels at T2 (post massage) were entered as predictors in step 1 and the interaction between emotional maltreatment and oxytocin levels T2 after massage in step 2.

## Results

### *Oxytocin levels*

The results from the hierarchical regression analysis with the contrast OT score as dependent variable are displayed in Table 1. The model was significant ( $F(3,40) = 3.16, p = .04$ ) and the effects of baseline oxytocin level ( $\beta = -.33, p = 0.04$ ) and emotional maltreatment ( $\beta = -.43, p = 0.01$ ) were both significant, indicating that baseline oxytocin level and maltreatment influenced changes in oxytocin level in response to massage. The interaction between emotional maltreatment and baseline OT level at the day of massage was not significant ( $\beta = -.25, p = 0.10$ ). A repeated measures Anova with time and condition as within-subject factors and emotional maltreatment group and baseline OT level group as between-subject factors was conducted to interpret the effects of baseline OT level and emotional maltreatment on OT level changes in response to massage. There was a significant main effect of time ( $F(1,41) = 5.28, p = .03$ , partial  $\eta^2 = .11$ ), but no significant main effect of condition ( $F(1,41) = 1.33, p = .26$ , partial  $\eta^2 = .03$ ) and no significant interaction between time and condition ( $F(1,41) = 1.87, p = .18$ , partial  $\eta^2 = .04$ ). The effect of baseline oxytocin level group was significant

( $F(1,41) = 10.65, p < .01$ , partial  $\eta^2 = .21$ ), but no significant main effect was found for emotional maltreatment group ( $F(1,41) = 2.73, p = .11$ , partial  $\eta^2 = .06$ ). Further, there was a significant three-way interaction between condition, time, and emotional maltreatment group ( $F(1,41) = 9.97, p < .01$ , partial  $\eta^2 = .20$ ) and a significant three-way interaction between condition, time, and baseline oxytocin level group ( $F(1,41) = 7.26, p = .01$ , partial  $\eta^2 = .15$ ). For individuals with low emotional maltreatment and for individuals with low baseline OT levels, there was a significant decrease in oxytocin levels in the control condition, whereas this decrease was absent in the massage condition (see Figure 2). The correlation between mean baseline OT level and emotional maltreatment was significant ( $r = -.42, p < .01$ ).

### *Handgrip force*

The repeated measures Anova with handgrip force ratio as dependent variable did not show main effects of massage versus control condition ( $F(1,33) = 2.49, p = .12$ , partial  $\eta^2 = .07$ ) or infant sound (laugh versus cry) ( $F(2,66) = 1.65, p = .20$ , partial  $\eta^2 = .05$ ) on handgrip force. The interaction between massage/control condition and infant sound was marginally significant ( $F(2,66) = 2.84, p = .07$ , partial  $\eta^2 = .08$ ). Furthermore, there was a marginally significant effect of emotional maltreatment on handgrip force ( $F(1,33) = 3.29, p = .08$ , partial  $\eta^2 = .09$ ) and a significant interaction between emotional maltreatment and massage condition ( $F(1,33) = 4.35, p < .05$ , partial  $\eta^2 = .12$ ). Massage reduced handgrip force ratio at baseline and during infant laughter and crying but only in individuals with experiences of maltreatment (see Figure 3). The three-way interaction between massage, infant sound condition, and emotional maltreatment was not significant ( $F(2,66) = 2.29, p = .11$ , partial  $\eta^2 = .07$ ).

The results from the hierarchical regression analysis with handgrip force ratio as dependent variable are displayed in Table 2. The model of the analysis with handgrip force in response to laughter was significant ( $F(3,33) = 2.98, p < .05$ ). Oxytocin levels after massage



were significantly related to handgrip force in response to laughter, with higher OT levels related to less excessive force ( $\beta = -.47, p = 0.02$ ), but there was no significant effect of emotional maltreatment ( $\beta = .12, p = 0.48$ ) and no significant interaction between oxytocin levels and emotional maltreatment ( $\beta = -.23, p = 0.21$ ). Results of the hierarchical regression analysis with handgrip force ratio in response to crying were similar. The model of the analysis with handgrip force in response to crying was marginally significant ( $F(3,33) = 2.54, p = .07$ ). Again, there was a significant effect of oxytocin levels after massage indicating an association between higher OT levels and less excessive force during crying ( $\beta = -.48, p = 0.02$ ), but no effect of emotional maltreatment ( $\beta = .03, p = 0.84$ ) and no significant interaction between OT level and emotional maltreatment ( $\beta = -.26, p = 0.16$ ).

To summarize, Study 2 showed that massage only stimulates oxytocin release in men with positive childhood experiences, but not in men with experiences of emotional maltreatment. In addition, high oxytocin levels after massage were related to reduced handgrip force during exposure to infant crying and laughter. This finding points to increased oxytocin release as one of the mechanism underlying the sensitivity enhancing effects of massage. Although massage did not affect oxytocin levels in individuals with experiences of maltreatment, it reduced the use of handgrip force in response to infant crying and laughter in these individuals, indicating that other mechanisms may underlie the positive effects of massage in maltreated individuals.

## Discussion

In two studies we examined the effects of a 15-minute massage applied by an electric massage seat cover on salivary oxytocin levels in women (Study 1) and men (Study 2). Compared to a control condition during which participants sat on a comfortable chair without massage, we

found that the massage affected oxytocin levels in both men and women. Our finding extends previous studies investigating the effects of massage by showing that massage *without* human touch results in elevated oxytocin levels compared to a control condition and that human touch is not an essential component in the oxytocin enhancing effects of massage. This finding converges with Meaney's (2001) work on rats showing that stroking pups with a brush mimics the tactile stimulation by maternal licking and grooming and down-regulates corticosterone levels. It also reminds us of Harlow's (1958) search for the essence of love in infant macaque monkeys residing in contact comfort of surrogate mothers.

In Study 2 we examined whether enhanced oxytocin levels after massage influence responding to infant signals and whether the effects of massage are dependent on childhood caregiving experiences. Interestingly, we found that higher oxytocin levels after massage were related to reduced handgrip force during exposure to infant crying and laughter. Individuals with high oxytocin levels after massage exerted less force than individuals with lower oxytocin levels. Together, these findings may indicate that massage promotes a more sensitive response to infant signals by stimulating oxytocin release. Thus, our findings point to increased oxytocin release as one of the mechanism underlying sensitivity enhancing effects of massage. Previous studies showed that intranasal oxytocin stimulates parental sensitive responsiveness to infants (Naber et al., 2012; Naber et al., 2010), possibly by enhancing empathy-related brain activity and inhibiting anxiety-related amygdala activity during exposure to infant crying and laughter (Riem et al., 2011; Riem et al., 2012). The current study indicates that the stimulation of endogenous oxytocin release through massage may be another way of promoting positive parent-infant interactions.

Our findings may have implications for the development of parenting interventions. Previous research indicates that intranasal oxytocin administration is not effective as a stand-alone intervention targeting psychiatric disorders and insensitive parenting (Bakermans-

Kranenburg & Van IJzendoorn, 2013). However, stimulation of endogenous oxytocin release might improve troubled parent-child relationships. Holt-Lunstad et al. (2011) showed that a 4-week intervention enhancing partner support through warm touch had stress-reducing effects and normalized oxytocin levels in individuals with depressive symptoms. Future studies should examine whether the stimulation of endogenous oxytocin release through massage promotes sensitive parent-infant interactions. Massage applied by a massage chair or seat cover may be an easy way of enhancing oxytocin levels in parents and possibly also in infants, which may in turn promote positive parent-infant interactions. Massage combined with intranasal oxytocin or a behavioral intervention may also be effective in stimulating sensitive parenting, for example in mothers with postpartum depression.

Unfortunately, massage increased oxytocin levels only in men with positive childhood experiences, but not in men with experiences of emotional maltreatment. Moreover, salivary oxytocin levels were lower in individuals with experiences of emotional maltreatment. This is consistent with previous studies showing that adverse childhood experiences lead to a dysregulation of the oxytocin system and reduced sensitivity to intranasal oxytocin (Fan et al., 2015; Meinschmidt & Heim, 2007; Riem et al., 2013). Thus, individuals with negative childhood experiences do not only show abnormal sensitivity to exogenous oxytocin administration, but also a different response to stimulation of endogenous oxytocin release. It has been suggested that negative childhood experiences change the oxytocin system, possibly through methylation of genetic areas regulating the oxytocin system and different expressions of oxytocin receptors in the brain (Kumsta et al., 2015), or through an increase in the density of vasopressin receptors at the cost of oxytocin receptors. Differences in oxytocin and vasopressin receptor expression may, in turn, lead to differential sensitivity to intranasal oxytocin and decreased sensitivity to stimulation of endogenous oxytocin release.

A limitation of our study is that our findings can only be generalized to individuals without children. Massage effects on oxytocin levels should be replicated in future studies in parents and with larger samples. Furthermore, the effects of the massage seat cover were not compared with human massage. Effects of massage with human touch might be more pronounced than effects of massage applied by a seat cover. Third, although we found that massage increased average oxytocin level, we did not find a significant change in the course of oxytocin levels across time in Study 1. In a previous study we found that salivary oxytocin levels remained elevated up to seven hours after intranasal OT administration (Van IJzendoorn et al., 2012). In Study 1 we assessed oxytocin levels up to three hours after the massage, which might be too short for the oxytocin levels to return to baseline. Future studies should cover a longer period of time in order to understand the duration of the effects of massage. Lastly, in the current study we did not find evidence for a sex specific oxytocin response to massage. However, the influence of emotional maltreatment on oxytocin response to massage was only examined in the male sample but not in the female sample. Animal studies indicate that variations in maternal care influence the expression of oxytocin receptors in a gender-specific manner (Francis et al., 2002). Future studies should therefore examine whether negative childhood experiences influence sensitivity to endogenous oxytocin release similarly in men and women.

A question that should be addressed in future research is how enhanced oxytocin levels after massage promote a more sensitive response to infant signals. One explanation is that oxytocin promotes affiliative and empathic responses. Alternatively, enhanced oxytocin levels after massage may reflect stress reduction as a result of the anxiolytic effects of oxytocin, which in turn promote a more sensitive response. Ideally, future studies should also examine whether affectionate touch or massage influences subjective and physiological stress responses, for example measured with cortisol. Animal studies have shown that central

oxytocin levels inhibit the Hypothalamic-Pituitary-Adrenal (HPA) axis (Neumann et al., 2000), which is in line with research showing that intranasal oxytocin administration results in cortisol decreases in humans (Cardoso et al., 2013; Heinrichs et al., 2003). Thus, oxytocin and cortisol interact in the response to stress and beneficial massage effects on caregiving responses may also be mediated by cortisol decreases. Previous research points to an important role of oxytocin as an underlying biological mechanism for stress-protective effects of positive social interactions. For example, oxytocin enhances positive effects of social support during stress (Heinrichs et al., 2003). Coan et al. (2006) showed that holding a partner's hand during stress reduces neural threat responses, suggesting that touch alleviates distress and improves stress regulation. Thus, oxytocin seems to be a likely candidate underlying the comforting effects of supportive touch during stress.

In conclusion, we are the first to examine effects of massage applied by an electric massage seat cover on salivary oxytocin levels in men and women in two exploratory pilot studies. Our findings seem to indicate that massage stimulates oxytocin release and that enhanced oxytocin levels after massage promote a more sensitive response to infant signals. However, we found that men with experiences of emotional maltreatment showed lower oxytocin levels, which did not increase after massage. These findings indicate that negative childhood experiences are associated with atypical responding to stimulation of endogenous oxytocin release and extends previous research showing a dysregulated oxytocin system after early adversity. Although massage did not increase oxytocin levels in men with experiences of emotional maltreatment, it normalized excessive handgrip force in response to infant crying and laughter in these individuals. This may indicate that, instead of increased oxytocin release, other mechanisms underlie the sensitivity enhancing effects of massage, for example reduced stress. Future studies should examine whether stimulation of endogenous oxytocin

release through massage affects parent-infant interactions and explore whether it can be an effective auxiliary intervention targeting insensitive parenting.

Table 1. Summary of hierarchical regression analysis with the contrast OT score as dependent variable, baseline oxytocin levels (T1) at the day of the massage condition and emotional maltreatment in the first step and the interaction between baseline oxytocin levels and emotional maltreatment in the second step.

	OT contrast score (massage - control)			
	B	SE	$\beta$	delta R <sup>2</sup>
Step 1				0.14*
Baseline OT	-0.49	0.23	-.33*	
Emotional maltreatment	-27.56	10.05	-.43**	
Step 2				0.06
Baseline OT x Emotional maltreatment	-5.25	3.16	-.25	

\*  $p < .05$  \*\*  $p < .01$ , Betas derived from the final block of the regression model.

Table 2. Summary of hierarchical regression analysis with handgrip ratio as dependent variable, oxytocin levels after massage (T2) and emotional maltreatment in the first step and the interaction between oxytocin levels after massage and emotional maltreatment in the

	Handgrip Ratio Laughter				Handgrip Ratio Crying			
	B	SE	$\beta$	delta R <sup>2</sup>	B	SE	$\beta$	delta R <sup>2</sup>
Step 1				0.18*				0.14 †
Oxytocin T2 (after massage)	-0.01	0.01	-.47*		-0.02	0.01	-.48*	
Emotional maltreatment	0.18	0.26	.12		0.05	0.27	.03	
Step 2				0.14				0.05
Oxytocin T2 x Emotional maltreatment	-0.07	0.06	-.23		-0.09	0.06	-.26	

second step.

†  $p < .1$ , \*  $p < .05$ , Betas derived from the final block of the regression model.



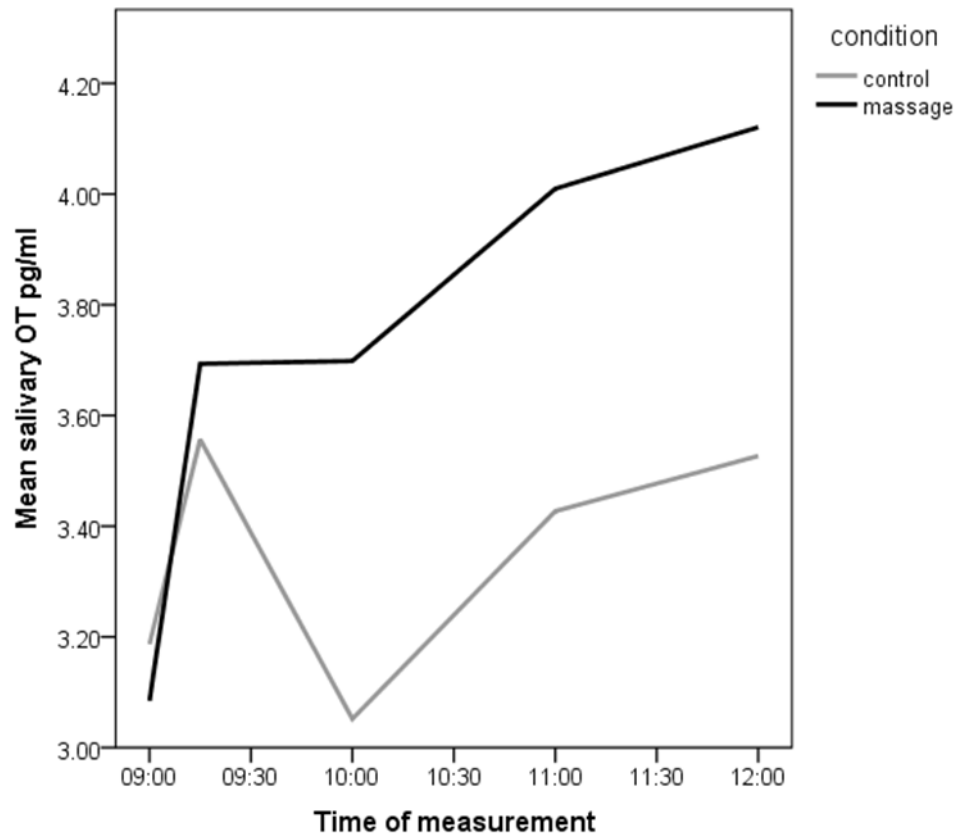


Figure 1. Observed mean values of oxytocin at the five measurement occasions for the massage and control condition (Study 1: female sample).

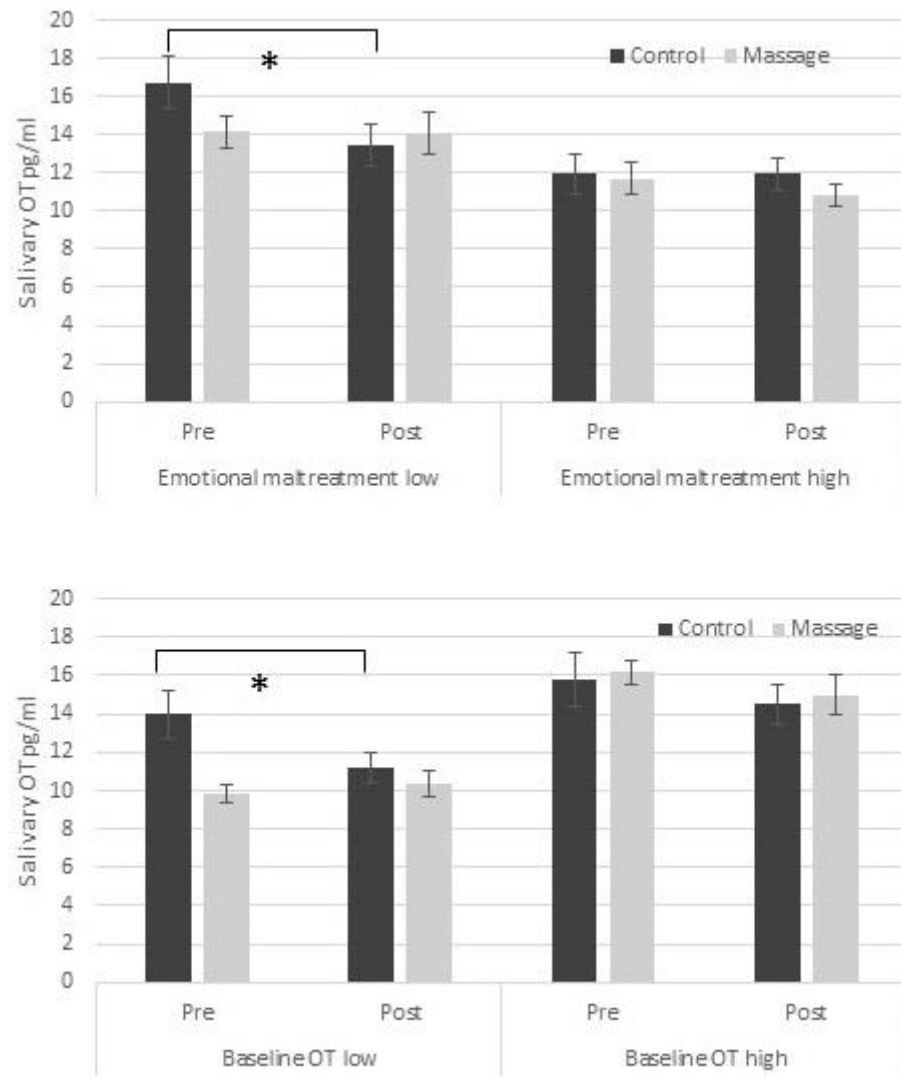


Figure 2. Mean (SE) salivary OT levels at T1 (pre message/control chair) and T2 (post message/control chair) in the control and massage condition for individuals with low and high emotional maltreatment (upper panel) and low and high baseline levels at the day of the massage condition (lower panel) (Study 2: male sample).

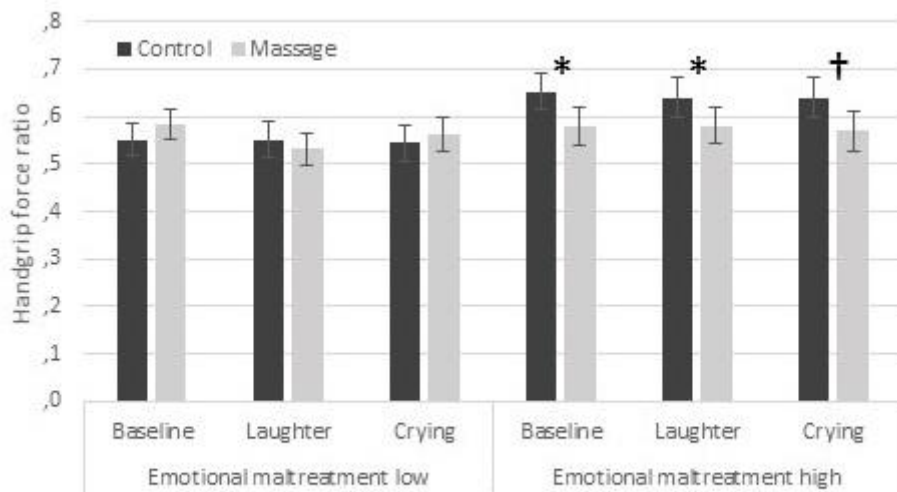


Figure 3. Mean (SE) handgrip force ratio at baseline and during infant laughter and crying in the control and massage condition for individuals with low and high emotional maltreatment (Study 2: male sample).

## References

- Bakermans-Kranenburg, M. J., & Van IJzendoorn, M. H. (2013). Sniffing around oxytocin: Review and meta-analyses of trials in healthy and clinical groups with implications for pharmacotherapy. *Transl Psychiatry*, 3, e258. doi:10.1038/tp.2013.34
- Bakermans-Kranenburg, M. J., van IJzendoorn, M. H., Riem, M. M., Tops, M., & Alink, L. R. (2012). Oxytocin decreases handgrip force in reaction to infant crying in females without harsh parenting experiences. *Social Cognitive and Affective Neuroscience*, 7(8), 951-957. doi:10.1093/scan/nsr067
- Barr, R. G., Trent, R. B., & Cross, J. (2006). Age-related incidence curve of hospitalized Shaken Baby Syndrome cases: Convergent evidence for crying as a trigger to shaking. *Child Abuse & Neglect*, 30(1), 7-16. doi:DOI 10.1016/j.chiabu.2005.06.009
- Cardoso, C., Ellenbogen, M. A., Orlando, M. A., Bacon, S. L., & Joober, R. (2013). Intranasal oxytocin attenuates the cortisol response to physical stress: a dose-response study. *Psychoneuroendocrinology*, 38(3), 399-407.
- Carter, C. S. (1998). Neuroendocrine perspectives on social attachment and love. *Psychoneuroendocrinology*, 23(8), 779-818. doi:S0306453098000559 [pii]
- Coan, J. A., Schaefer, H. S., & Davidson, R. J. (2006). Lending a hand: Social regulation of the neural response to threat. *Psychological Science*, 17(12), 1032-1039.
- Compier-de Block, L. H., Alink, L. R., Reijman, S., Werner, C. D., Maras, A., Rijnberk, C., . . . Bakermans-Kranenburg, M. J. (2015). Handgrip force of maltreating mothers in reaction to infant signals. *Child Abuse Negl*, 40, 124-131. doi:10.1016/j.chiabu.2014.03.006
- Ellingsen, D. M., Wessberg, J., Chelnokova, O., Olausson, H., Laeng, B., & Leknes, S. (2014). In touch with your emotions: oxytocin and touch change social impressions while others' facial expressions can alter touch. *Psychoneuroendocrinology*, 39, 11-20. doi:10.1016/j.psyneuen.2013.09.017
- Fan, Y., Pestke, K., Feeser, M., Aust, S., Pruessner, J. C., Böker, H., . . . Grimm, S. (2015). Amygdala-hippocampal connectivity changes during acute psychosocial stress: joint effect of early life stress and oxytocin. *Neuropsychopharmacology*, 40(12), 2736-2744.
- Feldman, R. (2012). Oxytocin and social affiliation in humans. *Hormones and Behavior*, 61(3), 380-391.
- Feldman, R. (2015). Sensitive periods in human social development: New insights from research on oxytocin, synchrony, and high-risk parenting. *Development and psychopathology*, 27(02), 369-395.
- Feldman, R., & Bakermans-Kranenburg, M. J. (2017). Oxytocin: a parenting hormone. *Current Opinion in Psychology*, 15, 13-18. doi:<https://doi.org/10.1016/j.copsyc.2017.02.011>
- Feldman, R., Gordon, I., Schneiderman, I., Weisman, O., & Zagoory-Sharon, O. (2010). Natural variations in maternal and paternal care are associated with systematic changes in oxytocin following parent-infant contact. *Psychoneuroendocrinology*, 35(8), 1133-1141. doi:S0306-4530(10)00029-6 [pii] 10.1016/j.psyneuen.2010.01.013
- Francis, D. D., Young, L. J., Meaney, M., & Insel, T. R. (2002). Naturally occurring differences in maternal care are associated with the expression of oxytocin and vasopressin (V1a) receptors: gender differences. *Journal of neuroendocrinology*, 14(5), 349-353.

- Gordon, I., Zagoory-Sharon, O., Leckman, J. F., & Feldman, R. (2010). Oxytocin, cortisol, and triadic family interactions. *Physiology & Behavior*, 101(5), 679-684. doi:10.1016/j.physbeh.2010.08.008
- Grewen, K. M., Davenport, R. E., & Light, K. C. (2010). An investigation of plasma and salivary oxytocin responses in breast- and formula-feeding mothers of infants. *Psychophysiology*, 47(4), 625-632. doi:10.1111/j.1469-8986.2009.00968.x
- Groh, A. M., & Roisman, G. I. (2009). Adults' Autonomic and Subjective Emotional Responses to Infant Vocalizations: The Role of Secure Base Script Knowledge. *Developmental Psychology*, 45(3), 889-893. doi:10.1037/A0014943
- Heim, C., Young, L. J., Newport, D. J., Mletzko, T., Miller, A. H., & Nemeroff, C. B. (2009). Lower CSF oxytocin concentrations in women with a history of childhood abuse. *Molecular psychiatry*, 14(10), 954-958. doi:10.1038/mp.2008.112
- Heinrichs, M., Baumgartner, T., Kirschbaum, C., & Ehlert, U. (2003). Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biological Psychiatry*, 54(12), 1389-1398.
- Holt-Lunstad, J., Birmingham, W., & Light, K. C. (2011). The influence of depressive symptomatology and perceived stress on plasma and salivary oxytocin before, during and after a support enhancement intervention. *Psychoneuroendocrinology*, 36(8), 1249-1256. doi:10.1016/j.psyneuen.2011.03.007
- Holt-Lunstad, J., Birmingham, W. A., & Light, K. C. (2008). Influence of a "warm touch" support enhancement intervention among married couples on ambulatory blood pressure, oxytocin, alpha amylase, and cortisol. *Psychosom Med*, 70(9), 976-985. doi:10.1097/PSY.0b013e318187aef7
- Kumsta, R., Hummel, E., Chen, F. S., & Heinrichs, M. (2015). Epigenetic regulation of the oxytocin receptor gene: implications for behavioral neuroscience. *Social Hormones and Human Behavior: What Do We Know and Where Do We Go from Here*, 19.
- Matthiesen, A. S., Ransjo-Arvidson, A. B., Nissen, E., & Uvnas-Moberg, K. (2001). Postpartum maternal oxytocin release by newborns: effects of infant hand massage and sucking. *Birth*, 28(1), 13-19. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11264623>
- Meinlschmidt, G., & Heim, C. (2007). Sensitivity to intranasal oxytocin in adult men with early parental separation. *Biological Psychiatry*, 61(9), 1109-1111. doi:10.1016/j.biopsych.2006.09.007
- Morhenn, V., Beavin, L. E., & Zak, P. J. (2012). Massage increases oxytocin and reduces adrenocorticotropin hormone in humans. *Altern Ther Health Med*, 18(6), 11-18. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/23251939>
- Naber, F., Poslawsky, I. E., van IJzendoorn, M. H., van Engeland, H., & Bakermans-Kranenburg, M. J. (2012). Brief Report: Oxytocin Enhances Paternal Sensitivity to a Child with Autism: A Double-Blind Within-Subject Experiment with Intranasally Administered Oxytocin. *Journal of Autism and Developmental Disorders*, 1-6. doi:10.1007/s10803-012-1536-6
- Naber, F., Van IJzendoorn, M. H., Deschamps, P., Van Engeland, H., & Bakermans-Kranenburg, M. J. (2010). Intranasal oxytocin increases fathers' observed responsiveness during play with their children: a double-blind within-subject experiment. *Psychoneuroendocrinology*, 35(10), 1583-1586. doi:S0306-4530(10)00097-1 [pii] 10.1016/j.psyneuen.2010.04.007
- Neumann, I., Wigger, A., Torner, L., Holsboer, F., & Landgraf, R. (2000). Brain oxytocin inhibits basal and stress-induced activity of the hypothalamo-pituitary-adrenal axis in

- male and female rats: partial action within the paraventricular nucleus. *Journal of neuroendocrinology*, 12(3), 235-244.
- Opacka-Juffry, J., & Mohiyeddini, C. (2012). Experience of stress in childhood negatively correlates with plasma oxytocin concentration in adult men. *Stress-the International Journal on the Biology of Stress*, 15(1), 1-10.
- Pierrehumbert, B., Torrisi, R., Laufer, D., Halfon, O., Ansermet, F., & Beck Popovic, M. (2010). Oxytocin response to an experimental psychosocial challenge in adults exposed to traumatic experiences during childhood or adolescence. *Neuroscience*, 166(1), 168-177. doi:<http://dx.doi.org/10.1016/j.neuroscience.2009.12.016>
- Reijneveld, S. A., Van der Wal, M. F., Brugman, E., Sing, R. A., & Verloove-Vanhorick, S. P. (2004). Infant crying and abuse. *Lancet*, 364(9442), 1340-1342. doi:S0140673604171912 [pii] 10.1016/S0140-6736(04)17191-2
- Riem, M. M., Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2016). Intranasal administration of oxytocin modulates behavioral and amygdala responses to infant crying in females with insecure attachment representations. *Attachment & Human Development*, 18(3), 213-234.
- Riem, M. M. E., Bakermans-Kranenburg, M. J., Pieper, S., Tops, M., Boksem, M. A. S., Vermeiren, R. R. J. M., . . . Rombouts, S. A. R. B. (2011). Oxytocin Modulates Amygdala, Insula, and Inferior Frontal Gyrus Responses to Infant Crying: A Randomized Controlled Trial. *Biological Psychiatry*, 70(3), 291-297. Retrieved from <http://www.sciencedirect.com/science/article/pii/S0006322311001399>
- Riem, M. M. E., Van IJzendoorn, M. H., Tops, M., Boksem, M. A., Rombouts, S. A., & Bakermans-Kranenburg, M. J. (2013). Oxytocin effects on complex brain networks are moderated by experiences of maternal love withdrawal. *Eur Neuropsychopharmacol*, 23(10), 1288-1295. doi:10.1016/j.euroneuro.2013.01.011
- Riem, M. M. E., van IJzendoorn, M. H., Tops, M., Boksem, M. A. S., Rombouts, S. A. R. B., & Bakermans-Kranenburg, M. J. (2012). No Laughing Matter: Intranasal Oxytocin Administration Changes Functional Brain Connectivity during Exposure to Infant Laughter. *Neuropsychopharmacology*, 37(5), 1257-1266. Retrieved from <http://dx.doi.org/10.1038/npp.2011.313>
- Rilling, J. K., DeMarco, A. C., Hackett, P. D., Chen, X., Gautam, P., Stair, S., . . . Patel, R. (2014). Sex differences in the neural and behavioral response to intranasal oxytocin and vasopressin during human social interaction. *Psychoneuroendocrinology*, 39, 237-248.
- Soltis, J. (2004). The signal functions of early infant crying. *Behavioral and Brain Sciences*, 27(4), 443-+. Retrieved from <Go to ISI>://000226860300001
- Taylor, S. E. (2006). Tend and Befriend. *Curr Dir Psychol Sci*, 15(6), 273-277. doi:10.1111/j.1467-8721.2006.00451.x
- Van IJzendoorn, M. H., Bhandari, R., Van der Veen, R., Grewen, K. M., & Bakermans-Kranenburg, M. J. (2012). Elevated salivary levels of oxytocin persist more than 7 h after intranasal administration. *Front Neurosci*, 6, 174. doi:10.3389/fnins.2012.00174
- Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect - the Panas Scales. *Journal of Personality and Social Psychology*, 54(6), 1063-1070. doi:Doi 10.1037/0022-3514.54.6.1063
- Weisman, O., Zagoory-Sharon, O., Schneiderman, I., Gordon, I., & Feldman, R. (2013). Plasma oxytocin distributions in a large cohort of women and men and their gender-specific associations with anxiety. *Psychoneuroendocrinology*, 38(5), 694-701.